REMARKS/ARGUMENTS

Claims 1-31 and 33 are pending and presented for examination. The Examiner has withdrawn claims 8-11, 17, 19, 20, 24 and 28-36 under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 32 and 34-36 were previously canceled, claims 30 and 33 are amended and claims 1-24, 28-29 and 31 are unchanged from the original presentation. Applicants believe these amendments add no new matter. Applicants reserve the right to pursue amended or canceled subject matter in divisional and/or continuation applications. Applicants acknowledge, with appreciation, the withdrawal of all of the rejection under 35 U.S.C. §§ 112, second paragraph. For the Examiner's convenience, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action. Reconsideration of the application is requested in view of the amendments to the claim set and the following remarks.

Rejection under 35 U.S.C. § 112, 1st paragraph

The Patent Office has rejected claims 30, 31 and 33 under 35 U.S.C. § 112 first paragraph, as allegedly failing the written description requirement. The Patent Office alleges that:

a) one of skill in the art could not identify any particular compound encompassed by the claims;

b) the specification does not clearly set forth the structure of the desired compounds;

c) the specification contains no structural or specific functional characteristics of those compounds which inhibit serine protease activity of matriptase or MTSP1, besides the compounds instantly disclosed; and

d) one of skill in the art would conclude that the "skilled artisan" was not in possession of the method of treating "an unspecified disease".

Applicants respectfully traverse the rejection because the specification sets forth:

(1) Established mechanisms for treating specific diseases by inhibiting serine protease activity of matriptase or MTSP1;

(2) A number assays which confirm the efficacy of the disclosed compounds; and

(3) A working example of one embodiment of the invention as claimed;

which demonstrates the Applicants had possession of the invention as currently claimed.

The legal standard for a written description rejection

According to the MPEP, to satisfy the written description requirement, a patent specification must merely describe the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *See Lockwood v. American Airlines, Inc.*, 41 USPQ2d 1961, 1966 (1997); *Vas Cath, Inc. v. Mazurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991). A specification may provide support in a variety of ways, including the disclosure of a working embodiment that meets all of the limitations of the claim. *See Cooper v. Goldfarb*, 47 USPQ2d 1896, 1901 (Fed. Cir. 1998). Possession of a claimed invention may be demonstrated by description of the invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. MPEP § 2163(I). Moreover, a strong presumption exists with regard to originally filed claims that an adequate written description of the claimed invention is present when the application is filed. MPEP § 2163(I)(A). In order to properly make a written description rejection, the Patent Office has the burden of presenting by preponderance of evidence why a person skilled in art would not recognize in Applicant's disclosure a description of the invention as defined by the claims. *See In re Wertheim*, 191 USPQ 90, 97 (CCPA 1976). Therefore, where the specification provides an actual reduction to practice of a process that meets all the limitations of the claim thereby demonstrating that the invention works for its intended purpose, the Patent Office must present evidence as to why one skilled in the art would not reasonably conclude that the inventor was in possession of the claimed method. *See* MPEP §2163 II.A.3.(a). In the present Office Action, the Patent Office has only asserted that the disease is "unspecified."

Recent case law concerning the written description requirement affirms that an applicant can properly obtain method claims to medical treatments based on the administration of chemical agents, especially where they are defined with a chemical structure. See *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63USPQ2d 1609, 1613 (Fed. Cir. 2002). In *Enzo*, the United States Court of Appeals for the Federal Circuit held that the written description requirement for method of treatment claims is satisfied when coupled with a disclosed correlation between that method and a structure that is "sufficiently known or disclosed." *Id.*

More recently, the Federal Circuit upheld the decision in *University of Rochester v. G.D. Searle & Co.*, where the U.S. District Court for the Western District of New York applied the standard set forth by the Federal Circuit in *Enzo* to claims covering a method of selectively inhibiting an enzyme using a pharmaceutical agent. The Federal Circuit stated "the written description requirement can be met by 'showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics,' including, *inter alia,* 'functional characteristics when coupled with a known or disclosed correlation between function and structure.'" *See, University of Rochester v. G.D. Searle & Co.*, 69 USPQ2d 1886 (Fed. Cir. 2004). The patent at issue in *Rochester* claimed a "method for selectively inhibiting PGHS-2 [mammalian prostaglandin H synthase-1] activity in a human host" using a "non-steroidal compound" in which "the activity of PGHS-1 is not inhibited." Only because the specification did not set forth a compound that would be suitable for use in practicing the claimed invention, did the Federal Circuit uphold the district court's decision of summary judgment invalidating the claims for failing to fulfill the written description requirement. *See University of Rochester v. G.D. Searle & Co.*, 69 USPQ2d 1886 (Fed. Cir. 2004).

It is apparent from *Enzo* and *Rochester* that an applicant can properly obtain method of treatment claims based on the administration of chemical agents defined by structure. According to the Federal Circuit, the required correlation between structure and function may be met by disclosing as few as three operable structures. *See Enzo Biochem Inc. v. Gen-Probe Inc.*, 63USPQ2d 1609, 1613 (Fed. Cir. 2002).

Previous evaluations of patent applications by the USPTO in the area of serine protease activity of matriptase or MTSP1 are consistent with the Federal Circuit's decisions

evaluating the written description requirement. The Patent Office's attention is directed to U.S. Patent No. 6,,677,377 and U.S. Patent No. 6,797,504 which the Examiner asserts in its double-patenting rejection, wherein similar method of treatment claims have issued with comparable or identical written description support.

Applicants respectfully assert that, in light of the Federal Court decisions outlined above, the current specification is more than adequate to meet the standard set forth by the Federal Circuit.

The specification sets forth established mechanisms for treating disease by inhibiting matriptase or MTSP1 with small molecules.

First, the methods of the presently claimed invention are not directed to an unspecified disease as the Patent Office alleges. Rather claims 30, 31 and 33 are directed to a method of treating a condition which is ameliorated by inhibiting or decreasing serine protease activity of matriptase or MTSP1. The language of the claims provides a functional definition of the disease.

The specification sets forth conditions recognized by those of skill in the art as treatable by inhibiting serine protease activity of matriptase or MTSP1, for example, at pages 1 to 8 and references cited therein. In contrast to the Patent Office's assertion, the specification describes what diseases may be treated and how to treat them, and specifically in the case of tumor growth, the specification describes which tumors may be reduced or inhibited. While not limited to the examples, Applicants describe how those of skill in the art recognized that the inhibition of serine protease activity of matriptase or MTSP1 has a role in tumor progression, migration and invasion and cancer metastasis, especially breast cancer, melanoma and tumors of the lung, bladder, stomach, cervix, ovary, kidney, brain, soft tissue, bone, prostate, rhabdomyosarcoma, retinoblastoma, Ewing sarcoma, neuroblastoma, osteosarcoma and leukemia, solid tumors and blood borne tumors, on pages 1-8 of the specification and references cited therein.

In contrast with the application in *Rochester*, the present specification sets forth a number of compounds which inhibit serine protease activity of matriptase or MTSP1, which are representative of the generic structural limitation of the method claims. *See* Figures 5A and B.

In light of the above, Applicants respectfully assert that the disclosure of this established mechanism, coupled with the teachings set forth in the specification as outlined herein, satisfies the legal requirements for obtaining method of treatment claims based on the administration of chemical agents which are specifically defined by their chemical structure.

The specification sets forth a number of assays which confirm the efficacy of the disclosed compounds

In addition, the specification sets forth a number of assays to evaluate the compounds for inhibiting serine protease activity of matriptase or MTSP1 and treating conditions which are ameliorated by inhibiting or decreasing serine protease activity of matriptase or MTSP1, specifically inhibiting or decreasing the growth of tumor cells. Serine protease activity of matriptase or MTSP1 was determined using a chromogenic substrate. *See* Example A. The ability of a compound to selectively inhibit matriptase activity is detected using a standard serine protease screen. *See* Example B. The ability of a compound to inhibit the growth of primary tumor cells or to reduce the occurrence of metastasis is detected using various animal models, such as a standard chicken embryo chorioallantoic model (CAM). *See* page 37. Other standard assays for evaluating a compound to inhibit the growth of primary tumor cells or to reduce the occurrence of metastasis are also disclosed, such as those described on pages 37-40 of the specification by L. Ossowski in *J. Cell Biol.* 107:2437-2445, 1998 or Brooks *et al. Methods in Molecular Biology* 129: 257-269, 1999.

These citations as set forth in the specification, demonstrate that such assays were well known in the art at the time of filing the application. The Patent Office has presented no evidence or reasoning as to why one skilled in the art would doubt the usefulness of the functional assays disclosed in the specification or well known in the art. Therefore, after examining the assays set forth in the specification and reviewing assays well known in the art, one skilled in the art would conclude that Applicants were in possession of methods for

inhibiting serine protease activity of matriptase or MTSP1 and treating conditions which are ameliorated by inhibiting or decreasing serine protease activity of matriptase or MTSP1, specifically inhibiting or decreasing the growth of tumor cells.

Disclosure of a Working Example

As mentioned above, a specification may provide support by including the disclosure of a working embodiment that meets all of the limitations of the claim. *See Cooper* at 1901. Furthermore, where the specification provides an actual reduction to practice of a process that meets all the limitations of the claim thereby demonstrating that the invention works for its intended purpose, the Patent Office must present evidence as to why one skilled in the art would not reasonably conclude that the inventor was in possession of the claimed method. *See* MPEP §2163 II.A.3.(a).

The specification provides a working example of the claimed invention in which serine protease activity of matriptase or MTSP1 is successfully inhibited by administering compounds of the invention. *See* Example A, pages 28-30. This example shows to those of skill in the art that the Applicant was in possession of this embodiment of the claimed invention as claimed works for its intended purpose. The Patent Office has presented no evidence or reasoning as to why one skilled in the art would doubt the validity of this experiment. Moreover, the Patent Office has presented no evidence or reasoning as to why one skilled in the art, after examining this experiment, would conclude that a inhibitor of serine protease activity of matriptase or MTSP1 would not work as intended in claims 30-31-33.

Applicants respectfully submit that one skilled in the art would recognize that Applicants were in possession of the methods as claimed. Therefore, in view of the above amendment and arguments, Applicants, respectfully request withdrawal of the rejection for alleged lack of written description.

Non-Statutory Double Patenting rejection

Claims 1-31 and 33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3 and 4 of U.S. Patent No. 6,797,504.

In response to the obviousness-type double patenting rejections over U.S. Patent Nos. 6,797,504, Applicants submit concurrently herewith a terminal disclaimer. Accordingly, Applicants respectfully request that this rejection be withdrawn..

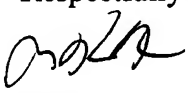
CONCLUSION

In view of the Office Action issued March 20, 2006, Applicant's believe no fee or petition for extension for time is required. However, if a fee and petition is required this is a request under 37 CFR 1.136(a) to extend the time of filing and the Commissioner is authorized to deduct such fee from the Deposit Account No. 20-1430. Please deduct any fees or credit any over payment to the above noted Deposit Account.

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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